

### **REMARKS**

The Office Action of June 17, 2009 presents the examination of claims 1-3 and 5-13. Claims 4 and 14-21 stand withdrawn after restriction of the claims.

Claim 4 is canceled herein, without prejudice to or disclaimer of the subject matter thereof. Claim 21 is also canceled herein, being directed to non-statutory subject matter (a "use").

Claims 12 and 13 are canceled, their subject matter having been incorporated into claims 1, 8 and 9 by the present amendments to the claims.

Claim 1 is further amended to recite a final concentration of calcium chloride in the medium. Support for this amendment is provided by the specification at least at page 18, lines 23-24 and in Figure 1.

#### **Rejection under 35 USC § 112, second paragraph**

Claims 5, 10 and 11 are rejected under 35 USC § 112, second paragraph as allegedly being indefinite. Claims 10 and 11 are canceled herein, rendering their rejection moot.

The Examiner objects to the language in claim 5 reciting a "locked" nucleic acid as a narrower embodiment of the more general "cross-linked" nucleic acid. Claim 5 is amended to recite only the term "locked" nucleic acid, thus obviating this rejection.

#### **Rejection under 35 USC § 112, first paragraph**

Claims 1-3 and 5-13 are rejected under 35 USC § 112, first paragraph, for alleged lack of enabling disclosure by the specification. In particular, the Examiner asserts that the claims must be limited in scope to use of calcium as the divalent metal ion and to a maximum concentration of 30.1 mM. Although Applicants do not particularly agree with this determination of the Examiner, claim 1 is amended to recite a range of concentration of calcium chloride in the medium, thus obviating this ground of rejection.

Rejections over prior art

Claims 1-3, 5, 6 and 8-13 are rejected under 35 USC § 103(a) as being unpatentable over Li '475 in view of Haberland (1999), Haberland (2000) and Chappel EP '362. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the present invention is not *prima facie* obvious over the combination of the cited references. The presently-claimed method is one in which the calcium salt is added to the medium after contacting the cells with a nucleic acid. (See, claim 1.) However, in each of the references cited, the calcium salt is added prior to or at the same time as contacting the cells with the nucleic acid (by mixing the nucleic acid with calcium chloride - see, Chappel EP '362). None of the references disclose the feature of the invention that the calcium salt is added after contacting the cell with the nucleic acid. Thus, no combination of the references discloses or suggests this feature of the invention, indeed the references teach away from the present invention, and so the combined references fail to establish *prima facie* obviousness of the invention. Accordingly, the instant rejection should be withdrawn.

Furthermore, even if deemed *prima facie* obvious, the present invention provides results unexpected by one of ordinary skill in the art who reads Li '475, Haberland (1999), Haberland (2000) and Chappel EP '362. In particular, the specification shows that nucleic acids could not be introduced into cells when the cell is previously contacted with calcium chloride as is done in the prior art cited. This is shown by Example 2 (page 19) and Figure 2 of the specification. On the other hand, when the cells are contacted with calcium chloride and then with the nucleic acid, efficient transfer of the nucleic acids to the cells is obtained. This is shown by Example 1 (page 18) and Figure 1.

Applicants submit that one of ordinary skill in the art who reads Li '475, Haberland (1999), Haberland (2000) and Chappel EP '362 would not expect that the addition of the calcium solution after contacting the cells with the nucleic acid would result in a large increase in efficiency of transfer of the nucleic acid into the cells, and that such result is objective evidence

of unobviousness sufficient to overcome any case of *prima facie* obviousness deemed to be established by these references. Accordingly, the instant rejection should be withdrawn.

Claim 7 is rejected under 35 USC § 103(a) as being unpatentable over Li '475 in view of Haberland (1999), Haberland (2000), Chappel EP '362 and Kubota '840. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The deficiencies of the first four references in failing to suggest the present invention are explained above. Kubota '840 is cited for disclosure of formulation of the nucleic acid with atelocollagen. However, Kubota '840 does not remedy the deficiencies of the other references with respect to their failure to suggest the present invention, and so the rejection of claim 7 over Li '475 in view of Haberland (1999), Haberland (2000), Chappel EP '362 and Kubota '840 fails for the same reasons as explained above, and should be withdrawn.

Applicants believe the pending application is in condition for allowance, and such favorable action is respectfully requested.


The period for response to the Office Action is extended by three months, to December 17, 2009, by petition filed herewith.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D., Reg. No. 36,623, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By   
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